IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	Curtiss III et al.	**Group No.:**	1645
Serial No.:	09/686,499	**Atty. Docket No.:**	53116-1192
Filed:	October 11, 2000		
For:	Functional Balanced-Lethal Host-Vector Systems	**Examiner:**	Khatol S. Shahnan Shah

Declaration of Roy Curtiss, III Pursuant to 37 C.F.R. §1.132

I, Roy Curtiss, III, declare and state as follows:

1. All of the statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true.

2. I am the inventor of the above identified patent application.

3. I am the first named inventor of U.S. Patent No. 6,024,961 and U.S. Patent No. 5,762,345.

4. I have reviewed the Office Action of 4/22/2004 in the instant application, and in particular the Patent Office's assertions that

(a) "Curtiss III et al. (U.S. Patent No. 6024961) disclose an avirulent immunogenic strain of Salmonella enterica serotype Typhi having a mutation in one or more genes.... They also teach a recombinant gene encoding the desired gene product. They disclose bacterial antigens. They also disclose recombinant vectors and desired gene product cytokine. The prior art discloses the claimed products."

(b) "...the Office does not have the facilities for examining and comparing applicant's products with the products of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art..."

5. The '961 patent, and the '345 patent incorporated by reference therein, do not disclose a recombinant complementing gene on an extrachromosomal vector, wherein the complementing gene can recombine to replace the non-functional native chromosomal essential gene, as required by the claims of the instant application.

6. Such replacement would require two reciprocal crossover events, which both demand as an obligate condition the existence of homologous sequences that flank the recombinant complementing gene and the non-functional native chromosomal essential gene.

7. All of the examples in the '961 patent and in the '345 patent utilize a complementing gene that cannot recombine to replace the non-functional native chromosomal gene. All of those examples were constructed in such a way that the DNA sequences flanking the non-functional native chromosomal essential gene lack homology with the sequences flanking the recombinant complementing gene, such that recombination is not possible.

8. A skilled artisan, at the time the instant application was filed, would have no reasonable expectation that a system comprising a non-functional native chromosomal essential gene and a recombinant complementing gene on a vector, wherein the complementing gene can recombine to replace the non-functional native chromosomal essential gene would function for its intended use. This is because a skilled artisan would believe that recombination would occur to render the system inoperative.

9. The experiments described in the examples of the instant application provide the first evidence that such a system does in fact function to stably maintain the desired gene (also carried on the vector comprising the recombinant complementing gene) in a progeny population of the microorganism.

10. I understand that willful false statements and the like are punishable by fine or imprisonment, or both (18 U.S.C. §1001) and may jeopardize the validity of the application or any patent issuing thereon.

Roy Curtiss, III, Ph.D.